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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/523,455	03/10/2000	Jurgen Engel	PM 264671	5040

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EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	18

DATE MAILED: 10/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/523,455	ENGEL ET AL.	
	Examiner	Art Unit	
	Shaojia A Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 19, 2003 has been entered in Paper No. 16.

This Office Action is a response to Applicant's request for continued examination (RCE) filed May 19, 2003 in Paper No. 16, and amendment filed May 19, 2003 which is the same amendment or the same copy of the amendment filed February 28, 2002 in Paper No. 9, and the response to the Final Office Action (mailed May 7, 2002), filed May 19, 2003 in Paper No. 17.

Currently, claims 1 and 3-24 are pending in this application.

Claims 1 and 3-24 are examined on the merits herein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 3-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Engel et al. (EP 0788 799, of record) and Albano et al. (of record) and Felberbaum et al. (of record) and Garfield (5,470,847, of record) in view of Deghenghi (5,945,128, of record) and Rabasseda et al. (of record) and Kent (4,016,259 of record) for reasons of record stated in the Office Action dated May 7, 2002 in Paper No. 10.

Engel et al. discloses that an LHRH-antagonist, such as cetrorelix, is useful in the method of suppression of premature ovulation in controlled ovarian sitmulation and assisted reproductive techniques, e.g., ICSI or intrauterine insemination by sperm injection, with multiple follicle and oocyte development. See the abstract, col. 1 lines 10-20, 30-34, 39-59, col. 2 lines 1-13, 16-25, col.3 lines 1-12, and claims 1-14. Engel et al. also discloses exogeneous stimulation of the ovarian follicle growth and ovulation induction with HCG, LHRH, or LHRH-agonists and the stimulation is performed by administration of FSH or HMG with or without recombinant LH. See Abstract, col. 2 lines 38-43. Engel et al. further discloses the effective amount of the LHRH-antagonist cetrorelix within the instant claim to be administered during luteal phase. See Examples claim 6-8. Finally, Engel et al. teaches progesterone is useful in supporting the beginning of pregnancy. See col.1 lines 23-24.

Albano et al. teaches that LHRH-antagonists, such as cetrorelix, are useful in the method of suppression of premature ovulation in controlled ovarian sitmulation and assisted reproductive techniques, e.g., IVF and ICSI, with multiple follicle and oocyte development, as well as the effective amount of the LHRH-antagonist cetrorelix within the instant claim to be administered during luteal phase. See Abstract, Introduction and

Results. Albano et al. further teaches that progesterone concentration is significantly lowered due to the administration of cetrorelix. See page 2115, 5th paragraph of right column.

Felberbaum et al. teaches that LHRH-antagonists, such as cetrorelix and ganirelix, are useful in the method of suppression of premature ovulation in controlled ovarian sitmulation and assisted reproductive techniques, e.g., IVF and ICSI, with multiple follicle and oocyte development, as well as the effective amount of the LHRH-antagonist cetrorelix within the instant claim to be administered during luteal phase. See Abstract, page 399-402 Felberbaum et al. further teaches a fall of sex steroids due to the administration of LHRH-antagonists. See page 398, the last three lines.

Garfield teaches that the administration of progestogen in the follicular phase is useful along with other progestins, an estrogen, e.g. ethinylestradiol, and an LHRH-antagonist in a method of controlling ovarian stimulation and preventing conception. See abstract, col.1 lines 18-67 and col.5 lines 35-38. Garfield also teaches that the ovarian stimulation is achieved with antioestrogens, such as clomiphene, combined with gonadotropins. See col. 2 lines 9-17, col.5 lines 64-67 and col.6 lines 30-40.

The prior art does not expressly disclose that the particular LHRH-antagonist are teverelix, antide, and abarelix and their effective amounts to be administered. The prior art does also not expressly disclose that the ovarian stimulation therapy may be on Fridays to Mondays, and ooctye pick up and ART may be undertaken on Mondays to Thursdays. The prior art does not expressly further disclose the particular employment

of oral contraceptive preparations containing progestogen and mestranol in the management of infertility.

Deghenghi discloses cetrorelix, teverelix, ganirelix and antide are known to be LHRH-antagonists. see col.2 lines 19-23.

Rabasseda et al. teach that LHRH-antagonists such as cetrorelix, ganirelix, and abarelix are known to be useful in the treatment of female infertility (see Introduction and Table 1 of page 397).

Kent discloses that the combination of progestogens and estrogen, i.e., mestranol and ethinylestradiol is useful in animal contraception (see col.1 lines 20-25).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular LHRH-antagonist such as teverelix, antide, and abarelix and to optimize their effective amounts to be administered, and to schedule or program the ovarian stimulation therapy on Fridays to Mondays and ooctye pick up and ART on Mondays to Thursdays, to employ the particular estrogen, mestranol, in oral contraceptive preparations along with progestogen.

One having ordinary skill in the art would have been motivated to employ the particular LHRH-antagonist such as teverelix, antide, and abarelix since teverelix, antide, and abarelix are known to be LHRH-antagonists, useful in the methods of controlled ovarian situmlation and assisted reproductive techniques and of the treatment of infertility according to Engel et al., Albano et al., Felberbaum et al., Deghenghi and Rabasseda et al. Additionally, one of ordinary skill in the art would have been motivated to optimize the effective amounts of active ingredients in the composition because the

optimization of amounts of active agents to be administered is considered well within the skill of artisan. One having ordinary skill in the art would have been motivated to schedule or program the ovarian stimulation therapy on Fridays to Mondays and ooctye pick up and ART on Mondays to Thursdays since scheduling or programming the known ovarian stimulation therapy for Fridays to Mondays according to the calendar is considered well within the skill of artisan as the optimization of a result effective parameter, e.g., dosage regimen. One having ordinary skill in the art would have been further motivated to employ the particular estrogen, mestranol, in oral contraceptive preparations along with progestogen in the management of infertility since the known contraceptive preparations of Kent contain mestranol and progestogen, and estrogen and progestin containing contraceptive agents are known broadly to be useful in the therapeutic management of infertility.

Since all method and composition components herein are known to be useful to treat or manage the infertility, it is considered prima facie obvious to combine them into a single method useful for the very same purpose. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

Applicant's remarks filed on May 19, 2003 in Paper No. 17 with respect to this rejection of claims 1 and 3-24 made under 35 U.S.C. 103(a) have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art for the following reasons.

Again, Applicant's arguments that the cited references, either alone or in combination does not render the presently claimed invention unpatentable have been considered but are not found persuasive.

Applicant asserts the citation of seven different and unrelated documents. Contrary to Applicant's assertion, all cited references, especially all primary references, Engel et al., Albano et al., Felberbaum et al. and Garfield, clearly disclose the methods of suppression of premature ovulation in controlled ovarian sitmulation and assisted reproductive techniques.

As discussed in the Final Rejection, the instant LHRH-antagonists such as teverelix, antide, and abarelix are known to be LHRH-antagonists and known to be useful in the methods of controlled ovarian situmlation and assisted reproductive techniques and of the treatment of infertility according to Engel et al., Albano et al., Felberbaum et al., Deghenghi and Rabasseda et al. Thus, each step in the instant claimed method is known in the prior art. It must be recognized that any judgment on obviousness takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made. See MPEP 2145.

Further, the particular estrogen herein, mestranol, in oral contraceptive preparations in combination with progestogen are well known contraceptive agents and also known broadly to be useful in the therapeutic management of infertility according to the prior art. Therefore, one of ordinary skill in the art would have reasonably expected that combining these particular agents known useful for the same purpose in a composition to be administered would produce additive therapeutic effects to improve

the treatment of in the therapeutic management of infertility, absent evidence to the contrary.

Since all active composition components herein are known to useful in the therapeutic management of infertility, it is considered prima facie obvious to combine them into a single composition to form a third composition useful for the very same purpose. At least additive therapeutic effects would have been reasonably expected based on the well settled principle set forth *In re Kerkhoven* regarding combination inventions. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 SPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

Therefore, motivation to combine the teachings of the prior art cited herein to make the present invention is seen. The claimed invention is clearly obvious in view of the prior art.

Applicant's results of the instant method (program) in the specification at page 4-5 herein have been fully considered with respect to the nonobviousness and/or unexpected results of the claimed invention over the prior art but are not deemed persuasive for the reasons below. The results provide no clear and convincing evidence of nonobviousness or unexpected results over the cited prior art since there is no side-by-side comparison with the closest prior art. Therefore, the evidence presented in specification herein is not seen to support the nonobviousness of the instant claimed invention over the prior art.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a). Therefore, said rejection is adhered to.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 3-24 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,319,192.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to a method of therapeutic management of infertility by intrauterine insemination consisting of substantially similar method steps and administering the same pharmaceutical agents, i.e. an LHRRH-antagonist such as cetrorelix, HCG, native LHRH, LHRH-agonists or recombinant LH.

The claims of the instant application is drawn to the method of therapeutic management of infertility by programming of controlled ovarian stimulation and assisted reproductive procedures the improvement.

One having ordinary skill in the art would clearly recognize that the method in the patent and the method in the instant application consisting of substantially similar method steps and administering the same pharmaceutical agents are seen to substantially overlap.

Thus, the instant claims 1 and 3-24 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,319,192.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (703) 305-1008. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
September 29, 2003